Role of miRNAs in Neuronal Differentiation from Human Embryonic Stem Cell-Derived Neural Stem Cells.

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Public Summary:

Scientific Abstract:
microRNAs (miRNAs) are important modulators in regulating gene expression at the post-transcriptional level and are therefore emerging as strong mediators in neural fate determination. Here, by use of the model of human embryonic stem cell (hESC)-derived neurogenesis, miRNAs involved in the differentiation from neural stem cells (hNSC) to neurons were profiled and identified. hNSC were differentiated into the neural lineage, out of which the neuronal subset was enriched through cell sorting based on select combinatorial biomarkers: CD15-/CD29(Low)/CD24(High). This relatively pure and viable subpopulation expressed the neuronal marker beta III-tubulin. The miRNA array demonstrated that a number of miRNAs were simultaneously induced or suppressed in neurons, as compared to hNSC. Real-time PCR further validated the decrease in levels of miR214, but increase in brain-specific miR7 and miR9 in the derived neurons. For functional studies, hNSC were stably transduced with lentiviral vectors carrying specific constructs to downregulate miR214 or to upregulate miR7. Manipulation of either miR214 or miR7 did not affect the expression of beta III-tubulin or neurofilament, however miR7 overexpression gave rise to enhanced synapsin expression in the derived neurons. This indicated that miR7 might play an important role in neurite outgrowth and synapse formation. In conclusion, our data demonstrate that miRNAs function as important modulators in neural lineage determination. These studies shed light on strategies to optimize in vitro differentiation efficiencies to mature neurons for use in drug discovery studies and potential future clinical applications.